

# Efficacy of Residence at Moderate Versus Low Altitude on Reducing Acute Mountain Sickness in Men Following Rapid Ascent to 4300 m

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## Abstract

Staab, Janet E., Beth A. Beidleman, Stephen R. Muza, Charles S. Fulco, Paul B. Rock, and Allen Cymerman. Efficacy of residence at moderate versus low altitude on reducing acute mountain sickness in men following rapid ascent to 4300 m. *High Alt Med Biol* 14:13–18, 2013.—To determine if residence at moderate (~2000 m) compared to low (<50 m) altitude reduces acute mountain sickness (AMS) in men during subsequent rapid ascent to a higher altitude. Nine moderate-altitude residents (MAR) and 18 sea-level residents (SLR) completed the Environmental Symptoms Questionnaire (ESQ) at their respective baseline residence and again at 12, 24, 48, and 72 h at 4300 m to assess the severity and prevalence of AMS. AMS cerebral factor score (AMS-C) was calculated from the ESQ at each time point. AMS was judged to be present if AMS-C was  $\geq 0.7$ . Resting end-tidal CO<sub>2</sub> (P<sub>ET</sub>CO<sub>2</sub>) and arterial oxygen saturation (Sao<sub>2</sub>) were assessed prior to and at 24, 48, and 72 h at 4300 m. Resting venous blood samples were collected prior to and at 72 h at 4300 m to estimate plasma volume (PV) changes. MAR compared to SLR: 1) AMS severity at 4300 was lower ( $p < 0.05$ ) at 12 h ( $0.50 \pm 0.69$  vs.  $1.48 \pm 1.28$ ), 24 h ( $0.15 \pm 0.19$  vs.  $1.39 \pm 1.19$ ), 48 h ( $0.10 \pm 0.18$  vs.  $1.37 \pm 1.49$ ) and 72 h ( $0.08 \pm 0.12$  vs.  $0.69 \pm 0.70$ ); 2) AMS prevalence at 4300 was lower ( $p < 0.05$ ) at 12 h (22% vs. 72%), 24 h (0% vs. 56%), 48 h (0% vs. 56%), and 72 h (0% vs. 45%); 3) resting Sao<sub>2</sub> (%) was lower ( $p < 0.05$ ) at baseline ( $95 \pm 1$  vs.  $99 \pm 1$ ) but higher ( $p < 0.05$ ) at 4300 at 24 h ( $86 \pm 2$  vs.  $81 \pm 5$ ), 48 h ( $88 \pm 3$  vs.  $83 \pm 6$ ), and 72 h ( $88 \pm 2$  vs.  $83 \pm 5$ ); and 4) PV (%) did not differ at 72 h at 4300 m in the MAR ( $4.5 \pm 6.7$ ) but was reduced for the SLR ( $-8.1 \pm 10.4$ ). These results suggest that ventilatory and hematological acclimatization acquired while living at moderate altitude, as indicated by a higher resting Sao<sub>2</sub> and no reduction in PV during exposure to a higher altitude, is associated with greatly reduced AMS after rapid ascent to high altitude.

**Key Words:** acute mountain sickness, hypobaric hypoxia, acclimatization, fluid balance, ventilatory response to hypoxia

## Introduction

ALTITUDE ACCLIMATIZATION REFERS TO A SERIES of physiologic responses to prolonged exposure to hypobaric hypoxia in low-altitude residents. These responses improve oxygen transport and delivery such that altitude illness is reduced and performance is improved (Fulco, 1988; Young and Young, 1988). Acute mountain sickness (AMS) is a syndrome that typically develops several hours after arrival at altitudes exceeding 2000 m, and is characterized by headache, nausea, vomiting, dizziness, fatigue, and insomnia. Un-

fortunately, military operations often require unacclimatized troops to ascend rapidly to higher altitudes and then immediately perform intense and sustained physical activity. The result is a substantial increase in the severity and prevalence of AMS (Roach et al., 2000) and a high probability of a life-threatening reduction in troop effectiveness (Rodway et al., 2011).

Previous studies have reported that long-term (3 months to life) moderate-altitude residence (i.e., 1500 to 2600 m) induces sustained ventilatory and hematologic responses that allow individuals (e.g., troops) to acclimatize to higher altitudes

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14. ABSTRACT <b>To determine if residence at moderate (*2000 m) compared to low (&lt; 50 m) altitude reduces acute mountain sickness (AMS) in men during subsequent rapid ascent to a higher altitude. Nine moderate-altitude residents (MAR) and 18 sea-level residents (SLR) completed the Environmental Symptoms Questionnaire (ESQ) at their respective baseline residence and again at 12, 24, 48, and 72 h at 4300m to assess the severity and prevalence of AMS. AMS cerebral factor score (AMS-C) was calculated from the ESQ at each time point. AMS was judged to be present if AMS-C was &lt; 0.7. Resting end-tidal CO2 (PETco2) and arterial oxygen saturation (Sao2) were assessed prior to and at 24, 48, and 72 h at 4300 m. Resting venous blood samples were collected prior to and at 72 h at 4300m to estimate plasma volume (PV) changes. MAR compared to SLR: 1) AMS severity at 4300 was lower (p &lt; 0.05) at 12 h (0.50 + 0.69 vs. 1.48 + 1.28), 24 h (0.15 + 0.19 vs. 1.39 + 1.19), 48 h (0.10 + 0.18 vs. 1.37 + 1.49) and 72 h (0.08 + 0.12 vs. 0.69 + 0.70); 2) AMS prevalence at 4300 was lower ( p &lt; 0.05) at 12 h (22% vs. 72%), 24 h (0% vs. 56%), 48 h (0% vs. 56%), and 72 h (0% vs. 45%); 3) resting Sao2 (%) was lower (p &lt; 0.05) at baseline (95 + 1 vs. 99 + 1) but higher (p &lt; 0.05) at 4300 at 24 h (86 + 2 vs. 81 + 5), 48 h (88 + 3 vs. 83 + 6), and 72 h (88 + 2 vs. 83 ? 5); and 4) PV (%) did not differ at 72 h at 4300m in the MAR (4.5 + 6.7) but was reduced for the SLR (-8.1 + 10.4). These results suggest that ventilatory and hematological acclimatization acquired while living at moderate altitude, as indicated by a higher resting Sao2 and no reduction in PV during exposure to a higher altitude, is associated with greatly reduced AMS after rapid ascent to high altitude.</b>					
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more rapidly than sea-level residents (SLR) (Boning et al., 2001; Brothers et al., 2007; Brothers et al., 2010; Muza et al., 2004; Reeves et al., 1993; Schmidt et al., 2002). Previous studies, for example, reported a smaller decrement in both maximal and prolonged exercise performance in the first few days following rapid ascent to 4300 m in moderate-altitude residents (MAR) compared to SLR (Fulco et al., 2005; Fulco et al., 2007; Maresh et al., 1983). The degree that the severity and prevalence of AMS might also be improved at a higher altitude by first living for prolonged periods of time at moderate altitudes is largely unknown.

Several studies of short-term (i.e., 2–6 days) residence at moderate altitudes of 1600–3400 m have indicated that AMS is reduced by 20%–60% during the first few days at a higher altitude (Beidleman et al., 2009; Hansen et al., 1967; Stamper et al., 1980); presumably, longer-term moderate-altitude residence should reduce AMS symptoms even more, since many physiologic and hematologic adaptations may take as long as 17 months to develop fully at moderate altitude (Brothers et al., 2007). This hypothesis, however, has never been systematically and quantitatively assessed.

Therefore, the purpose of this study was to determine the extent that beneficial ventilatory and hematologic adaptations resulting from long-term (i.e., 5–46 months) moderate-altitude residence (i.e., 1800–2200 m) would reduce AMS severity and prevalence over the first several days at 4300 m following rapid ascent. To that end, we retrospectively analyzed data from two previous studies of SLR and MAR rapidly exposed to 4300 m that were conducted by our laboratory using identical procedures, equipment, and facilities (Fulco et al., 2007; Hagobian et al., 2006).

## Methods

### Study volunteers

Nine active duty military men (mean  $\pm$  SD; 30  $\pm$  3 yr, 74  $\pm$  6 kg, 179  $\pm$  5 cm, 41  $\pm$  5 mL/kg/min) living in Colorado Springs, CO (MAR) and 18 physically active men (25  $\pm$  5 yr, 78  $\pm$  8 kg, 179  $\pm$  5 cm, 57  $\pm$  7 mL/kg/min) living in the vicinity of Palo Alto, CA (SLR) volunteered to participate in these two studies. Prior to the study, MAR resided at 1800 to 2200 m for a mean of 21  $\pm$  3 mo (range: 5–46 months) while the SLR had not resided at altitudes greater than 2000 m for the 6 months immediately prior to the study. All participated in regular physical training for 3 to 6 days a week. All were nonsmokers and in good health as determined by medical history and evaluation. Each provided written informed consent before participating. Both studies were approved by the institutional review board (IRB) at the U.S. Army Research Institute of Environmental Medicine. The MAR study was also approved by the IRB for the U.S. Air Force Academy (USAFA) and the SLR study was approved by the IRB for the Veterans' Administration Palo Alto Health Care System (VAPAHCS). Investigators adhered to the policies for protection of human subjects as prescribed in Army Regulation 70-25 and the research was conducted in adherence with the provisions of 32 CFR Part 219.

### Study overview

Both studies used a prospective design in which the participants were first evaluated at their respective baseline residence and then evaluated again following a rapid ascent to

the same laboratory located at the summit of Pikes Peak, CO (4300 m, 458–464 mmHg).

### MAR study design

The MAR reported on 3 separate days to the Human Performance Laboratory at the USAFA (2200 m, 589–596 mmHg) for testing, which was conducted in a room maintained at a temperature and relative humidity of 21  $\pm$  2°C and 45  $\pm$  5%, respectively. Volunteers were familiarized with all test procedures on day 1, AMS and body weight (BW) measurements were conducted after the first morning void each day, peak oxygen uptake ( $\dot{V}O_{2peak}$ ) was assessed on a cycle ergometer on day 2, and resting blood samples and ventilation measurements were collected on day 3. One to two weeks following testing at the USAFA, the MAR were driven by automobile to the summit of Pikes Peak in less than 2 hours. Approximately 2 hours after arrival, a prolonged (i.e., 2–3 h) cycle exercise test ( $\sim$ 55% of altitude-specific  $\dot{V}O_{2peak}$ ) was conducted to simulate the duration and intensity of activity typical of mountain military operations (Rodway et al., 2011). Arterial oxygen saturation ( $SAO_2$ ) was recorded by pulse oximetry (Nonin Model 8600, Plymouth, MN) every 15 min during exercise, and the overall mean was recorded. Exercise test results were previously reported for the MAR (Fulco et al., 2007). AMS was assessed at 4300 m at 12, 24, 48, and 72 hours; resting ventilation at 24, 48, and 72 h; resting hemoglobin concentration ([Hb]) and hematocrit (Hct) at 72 h and sleep  $SAO_2$  and heart rate (HR) during the first night at 4300 m.

### SLR study design

The SLR reported on 3 separate days to the Clinical Studies Unit at the VAPAHCS (15 m, 748–762 mmHg) for testing in a room where the temperature and relative humidity were maintained at 21  $\pm$  2°C and 45  $\pm$  5%, respectively. Volunteers were familiarized with all test procedures on day 1, AMS and BW measurements were conducted after the first morning void each day,  $\dot{V}O_{2peak}$  was assessed on day 2, and resting blood samples and ventilation measurements were collected on day 3. Approximately 6 weeks after the baseline phase, volunteers were flown to Colorado Springs, CO (1850 m, 600–606 mmHg) where they spent the night in an apartment while breathing supplemental oxygen to maintain  $SAO_2$  at baseline levels ( $>$ 96%). The next morning, volunteers were driven to the summit of Pikes Peak while still breathing oxygen. Indoor temperature and humidity of the laboratory was 20  $\pm$  2°C and 40  $\pm$  5%, respectively. Upon arrival on the summit, oxygen was discontinued and the same testing procedures were followed as described above for MAR.

### Altitude-illness assessment

AMS severity and prevalence were assessed at baseline in the morning and again at 4300 m at 12, 24, 48, and 72 h using the shortened electronic version (Beidleman et al., 2007) of the Environmental Symptoms Questionnaire (ESQ) (Sampson et al., 1994). The ESQ was used to quantify a weighted AMS cerebral factor score (AMS-C) to assess AMS severity. At each time point, AMS was judged to be present if an individual's AMS-C score was  $\geq$  0.7 (Sampson et al., 1994).

### Ventilatory and cardiovascular assessment

Resting ventilation was measured in the morning prior to breakfast at baseline residence and at 24, 48, and 72 h at

4300 m. Volunteers sat in a semi-recumbent position and breathed through a low-resistance breathing circuit connected to a breath-by-breath open circuit metabolic system (Vmax 229, Sensormedics Inc., Yorba Linda, CA) calibrated with certified gases and volume standard. Each volunteer's resting minute ventilation ( $\dot{V}_E$ ), and end-tidal oxygen and carbon dioxide partial pressure ( $P_{ET}O_2$  and  $P_{ET}CO_2$ ) were measured. Simultaneously,  $SpO_2$  and HR were measured by pulse oximetry (Nonin Model 8600). Ventilation data were collected for at least 10 min with the mean over the last 5–8 min of the session calculated and used in the analyses. Resting systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured after completing ventilatory measures and mean arterial pressure (MAP) was calculated as  $0.333 (SBP - DBP) + DBP$ .

#### Hematologic assessment

Immediately following the resting ventilation measurements at baseline and at 72 h at 4300 m, venous blood samples were obtained from the forearm without stasis for the measurement of [Hb] and Hct. The samples were analyzed immediately in duplicate using the i-STAT portable clinical analyzer (Abbott Diagnostics, Abbott Park, IL). Percent change in plasma volume (PV) from baseline residence values to 4300 m was calculated according to the Dill equation (Dill and Costill, 1974).

#### Sleep assessment

During the first night at 4300 m, volunteers wore a small pulse oximeter (Nonin model 3100) on the nondominant wrist with an adhesive finger sensor that measured and recorded  $SpO_2$  and HR continuously (beat by beat) averaging over the entire sleep period. Two volunteers in the MAR group and four volunteers in the SLR group did not complete the sleep assessment due to equipment malfunction.

#### Statistical analyses

For all measurements, a two-way mixed factorial repeated measures ANOVA was used to analyze differences between the independent group factor (MAR vs. SLR) and test conditions (baseline residence, and the 12<sup>th</sup>, 24<sup>th</sup>, 48<sup>th</sup>, and 72<sup>nd</sup> h at 4300 m using Statistica v11.0 (Statsoft, Tulsa, OK). Significant main effects and interactions were analyzed using Tukey's least significant difference test. The Cochran's Q test was used to evaluate differences in the prevalence of AMS over test conditions within each group. For all tests, statistical significance was set at  $p < 0.05$ . Data are presented as means  $\pm$  SD when appropriate.

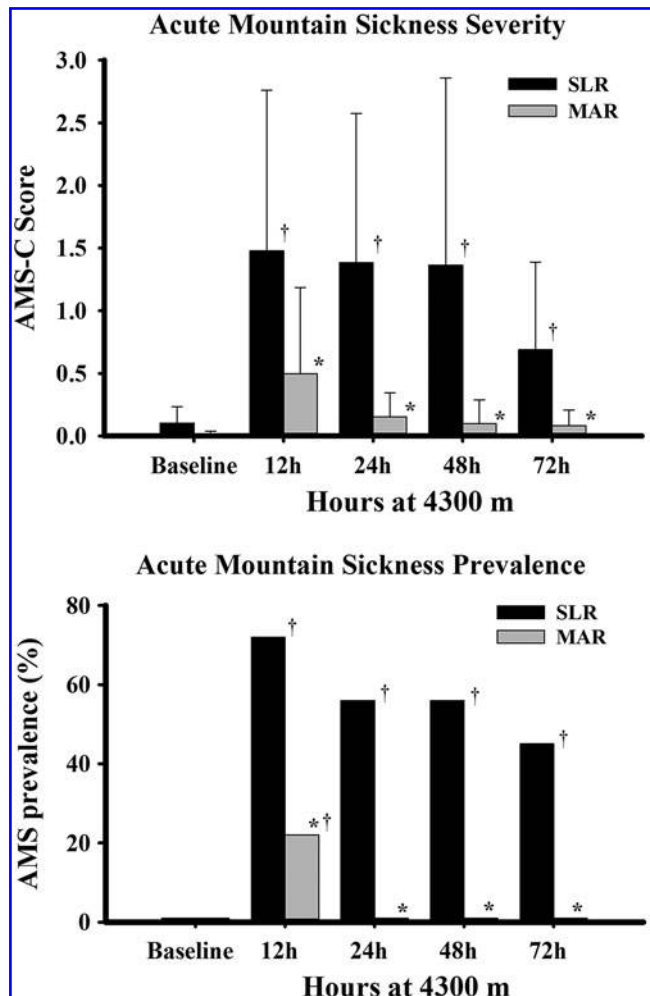
## Results

#### Altitude-illness measures

There were no significant differences in AMS-C scores between MAR and SLR, and no individuals in either group had scores indicative of AMS at baseline (Fig. 1). Both AMS-C scores and the prevalence of AMS were significantly lower in the MAR compared to the SLR throughout the altitude exposures (Fig. 1).

#### Resting ventilatory and cardiovascular measures of acclimatization

Both ventilatory and cardiovascular measures were higher in the MAR group relative to the SLR group at baseline (Table 1).



**FIG. 1.** Acute mountain sickness severity scores (AMS-C) and prevalence (%) of moderate-altitude residents (MAR) and sea-level residents (SLR) at their baseline residence and on the summit of Pikes Peak (4300 m) after 12, 24, 48, and 72 hours. Values for AMS-C are presented as mean  $\pm$  SD, and values for AMS prevalence are presented as proportions. \* $p < 0.05$  between groups; † $p < 0.05$  from baseline.

In addition, ventilatory and cardiovascular measures were increased in both groups in the first few days at 4300 m, but the increase was less dramatic in the MAR.  $P_{ET}CO_2$  was lower in the MAR group at baseline compared to the SLR group (Table 1). Both groups had lower  $P_{ET}CO_2$  values throughout the exposure to 4300 m compared to their respective baseline. At 4300 m, the MAR had a lower  $P_{ET}CO_2$  compared to the SLR at 24 h, but the values were similar at 48 and 72 h (Fig. 2). Resting  $SpO_2$  was  $\sim 6\%$  higher in the MAR compared to the SLR at 24, 48, and 72 h (Fig. 2) while resting HR and MAP were higher in MAR compared to SLR only at baseline (Table 1).

#### Exercise and sleep arterial oxygen saturation

In the first few hours at 4300 m during exercise,  $SpO_2$  was higher in the MAR compared to the SLR ( $79\% \pm 3\%$  vs.  $74\% \pm 6\%$ ). Similarly, overall mean sleep  $SpO_2$  during the first night at 4300 m was higher in the MAR compared to the SLR ( $81\% \pm 1\%$  vs.  $74\% \pm 6\%$ ). Overall mean sleep HR (bpm) on the first night at 4300 m was also lower in the MAR compared to the SLR ( $66 \pm 6$  vs.  $76 \pm 11$ ).

TABLE 1. RESTING VENTILATORY AND CARDIOVASCULAR INDICES OF ACCLIMATIZATION AT BASELINE RESIDENCE AND AT 24, 48, AND 72 H AT 4300 M FOR SEA-LEVEL RESIDENTS (SLR) AND MODERATE-ALTITUDE RESIDENTS (MAR)

Variable	Baseline		24 h		48 h		72 hrs	
	SLR	MAR	SLR	MAR	SLR	MAR	SLR	MAR
P <sub>ET</sub> O <sub>2</sub> (mmHg)	103.6±3.5	73.8±1.9*	51.6±4.7 <sup>†</sup>	50.1±2.1 <sup>†</sup>	52.5±3.2 <sup>†</sup>	52.5±2.4 <sup>†</sup>	52.7±3.6 <sup>†</sup>	53.1±1.5 <sup>†</sup>
P <sub>ET</sub> CO <sub>2</sub> (mmHg)	40.5±2.0	34.5±1.6*	31.9±2.8 <sup>†</sup>	30.1±1.3* <sup>†</sup>	30.0±2.3 <sup>†</sup>	29.2±1.8 <sup>†</sup>	29.9±2.4 <sup>†</sup>	28.1±1.8 <sup>†</sup>
VE (L/min)	9.1±1.6	10.1±1.6	14.0±3.9 <sup>†</sup>	11.5±1.9 <sup>†</sup>	14.7±4.5 <sup>†</sup>	11.9±1.7 <sup>†</sup>	14.2±3.7 <sup>†</sup>	12.3±2.1 <sup>†</sup>
VO <sub>2</sub> (L/min)	0.23±0.03	0.21±0.02	0.25±0.04	0.20±0.03*	0.25±0.04	0.22±0.03	0.25±0.05	0.21±0.03*
VCO <sub>2</sub> (L/min)	0.18±0.03	0.18±0.01	0.21±0.05 <sup>†</sup>	0.18±0.04	0.21±0.04 <sup>†</sup>	0.20±0.04 <sup>†</sup>	0.20±0.05 <sup>†</sup>	0.19±0.03
VE/VO <sub>2</sub> (L/min)	39.5±6.1	48.4±8.7	56.3±12.3 <sup>†</sup>	57.0±9.9 <sup>†</sup>	59.6±13.7 <sup>†</sup>	55.4±9.5 <sup>†</sup>	57.9±14.9 <sup>†</sup>	58.9±8.7 <sup>†</sup>
VE/VCO <sub>2</sub> (L/min)	50.7±8.0	57.4±11.1	68.2±14.4 <sup>†</sup>	67.1±16.9 <sup>†</sup>	71.3±15.1 <sup>†</sup>	60.1±13.3	71.1±15.9 <sup>†</sup>	65.1±10.9 <sup>†</sup>
RER	0.78±0.04	0.85±0.03*	0.83±0.08	0.87±0.10	0.84±0.05 <sup>†</sup>	0.93±0.09* <sup>†</sup>	0.81±0.07	0.91±0.10* <sup>†</sup>
SaO <sub>2</sub> (%)	99±1	95±1*	81±5 <sup>†</sup>	86±2* <sup>†</sup>	83±6 <sup>†</sup>	88±3* <sup>†</sup>	83±5 <sup>†</sup>	88±2* <sup>†</sup>
HR (bpm)	52±7	64±6*	75±9 <sup>†</sup>	75±8 <sup>†</sup>	75±12 <sup>†</sup>	70±9 <sup>†</sup>	74±10 <sup>†</sup>	67±11
MAP (mmHg)	86±4	91±5*	93±6 <sup>†</sup>	92±3	93±6 <sup>†</sup>	92±6	93±4 <sup>†</sup>	94±3

HR, heart rate; MAP, mean arterial pressure; P<sub>ET</sub>CO<sub>2</sub>, partial pressure of end-tidal carbon dioxide; P<sub>ET</sub>O<sub>2</sub>, partial pressure of end-tidal oxygen; RER, respiratory exchange ratio; SaO<sub>2</sub>, arterial oxygen saturation; VE, minute ventilation; VCO<sub>2</sub>, volume carbon dioxide produced; VE/VO<sub>2</sub>, ventilatory equivalent for oxygen, VE/VCO<sub>2</sub>, ventilatory equivalent for carbon dioxide; VO<sub>2</sub>, volume oxygen consumed. Values are mean±SD; \**p*<0.05 between groups; <sup>†</sup>*p*<0.05 from baseline.

#### Resting hematologic measures of acclimatization

The [Hb] (g/dl) and Hct (%) were higher at baseline in the MAR (16.1±0.8 and 47.1±1.9) compared to the SLR (15.0±1.0 and 45.1±2.9). [Hb] and Hct increased from baseline to 72 h for the SLR (15.8±1.0 and 47.1±2.7) but not the MAR (15.7±0.5 and 46.1±1.4), resulting in an estimated PV reduction for the SLR (−8.1±10.4%) but not the MAR (4.5±6.7%). The change in PV at 72 h at 4300 m was significantly different between groups (*p*=0.002).

#### Discussion

Retrospective analysis of data from our two previous studies conducted using similar experimental procedures showed that the ventilatory and hematologic adaptations acquired while living at moderate altitude were associated with reduced AMS prevalence and symptom scores compared to low altitude residents following a rapid ascent to 4300 m. Symptoms scores were reduced by ~70% to 90% in MAR compared to SLR, and AMS was completely absent in the MAR group after 24 h at 4300 m. This effect is more than the 46% reduction in AMS symptom scores observed in another study following a 6-day residence at the same moderate altitude prior to ascent to 4300 m (Beidleman et al., 2009). The ventilatory and hematologic adjustments induced by long-term moderate-altitude residence, as evidenced by a higher resting ventilation and [Hb] at the baseline residence and the subsequent higher resting, exercise, and sleep SaO<sub>2</sub> at 4300 m likely contributed to the lower AMS in the MAR compared to SLR during the first 72 h of exposure to 4300 m (Beidleman et al., 2004; Roach et al., 1998). Maresh et al. (1983) reported that AMS symptoms were reduced in moderate-altitude natives following ascent to 4270 m in a hypobaric chamber for 2 days, but AMS was never quantitated. Muza et al. (2004) also reported lower AMS symptom scores in MAR after 1 h of exposure to 4300 m, but the observations were not extended beyond that time period to determine if the differences in AMS scores persisted. Nevertheless, the results from both studies (Maresh et al. (1983) and Muza et al. (2004)) are consistent with our results.

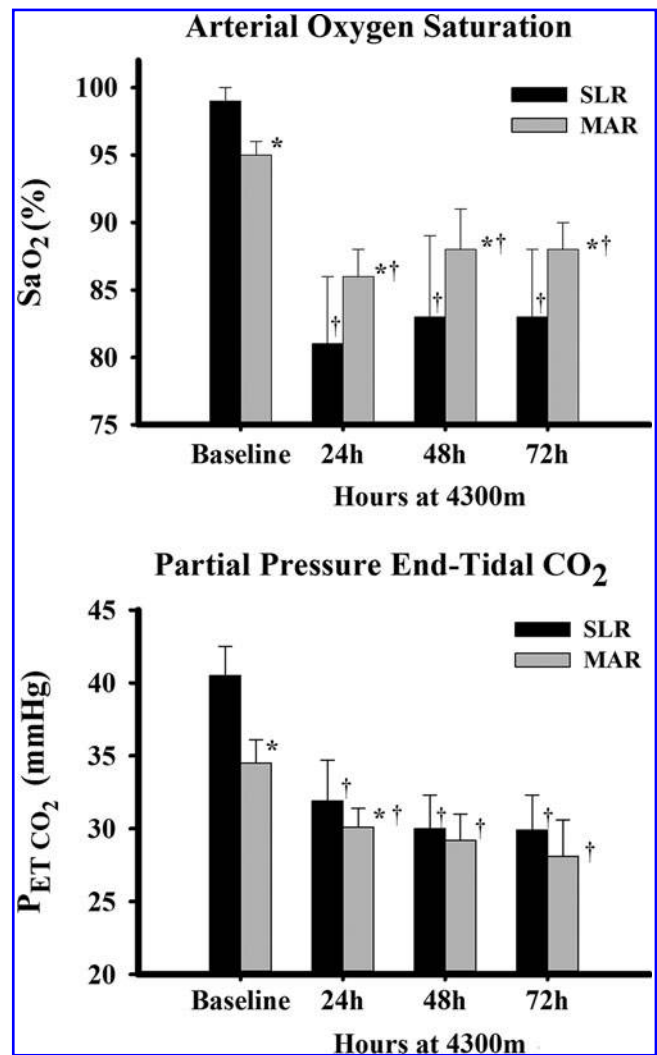


FIG. 2. Arterial oxygen saturation (SaO<sub>2</sub>) and partial pressure of end-tidal carbon dioxide (P<sub>ET</sub>CO<sub>2</sub>) of moderate-altitude residents (MAR) and sea-level residents (SLR) at their baseline residence and on the summit of Pikes Peak (4300 m) after 24, 48, and 72 hours. Values are presented as mean±SD; \**p*<0.05 between groups; <sup>†</sup>*p*<0.05 from baseline.



The ventilatory changes induced by moderate-altitude residence in this study are similar to those reported by others for men and women residing at similar altitudes (Maresh et al., 1988; Muza et al., 2004; Reeves et al., 1993). At baseline, we observed a ~15% higher resting alveolar ventilation, as reflected by a lower  $P_{ETCO_2}$ , in the MAR compared to the SLR. Two other studies reported a 11%–13% higher resting ventilation, as reflected by  $P_{ETCO_2}$ , in MAR (i.e., 1600 to 1940 m) compared to SLR also when measured at their baseline residence (Muza et al., 2004; Reeves et al., 1993). Our findings and the results from other studies suggest that significant ventilatory acclimatization is obtained while residing at moderate altitude.

During the first 72 h of exposure to 4300 m, the MAR in the present study maintained a ~5% lower level of resting  $P_{ETCO_2}$  compared to the SLR. Our findings are consistent with previously published work at the same altitude (Muza et al., 2004; Reeves et al., 1993) and indicate that the ventilatory acclimatization obtained during residence at moderate altitude is not only maintained but beneficial during at least the first 3 days of exposure to 4300 m. As a consequence of ventilatory acclimatization,  $SaO_2$  during rest, exercise, and sleep were also 6% to 9% higher in MAR compared to SLR during the first 24 h at 4300 m. Two previous studies reported a 2% to 5% higher resting  $SaO_2$  in MAR compared to SLR in the first 24 h at 4300 m (Muza et al., 2004; Reeves et al., 1993), but exercise and sleep  $SaO_2$  were not measured in these studies. This is the first study to our knowledge to demonstrate that there is increased ventilation in MAR compared to SLR not only during rest but also during exercise and sleep. Increased ventilation and higher  $SaO_2$  during exercise and sleep likely contributed to the 70%–90% reduction in AMS in the MAR.

The MAR also had a 7% higher [Hb] than the SLR when measured at baseline. This finding is consistent with the results of others that have reported that MAR living at 1800 to 2600 m have a 6%–13% higher [Hb] than SLR measured at their respective residence or shortly after arriving at moderate altitude (Boning et al., 2001; Brothers et al., 2007; Brothers et al., 2010; Maresh et al., 1985; Schmidt et al., 2002). The MAR in the present study did not maintain the ~7% elevated [Hb] compared to the SLR when measured at 72 h of exposure to 4300 m. In fact, both groups reached the same [Hb] and Hct values at 72 h of exposure because only the SLR lost PV. Some reports have suggested that AMS is related to acute impairments in fluid balance regulation during exposure to high altitude (Loeppky et al., 2005a; Loeppky et al., 2005b; Westerterp et al., 1996). The observation that MAR have already achieved body fluid homeostasis prior to exposure to a higher altitude may put them at less risk for developing AMS.

The conclusions resulting from this study may be limited due to the following conditions: 1) this was a retrospective analysis of two studies that were not originally designed with the present purpose in mind; 2) the analysis was conducted only on men; and 3) although physical fitness has not been shown to impact AMS, the  $\dot{V}O_{2peak}$  was higher in the SLR compared to the MAR, even adjusting for the elevation. Nevertheless, the implications of this retrospective analysis are clear for the millions of people who travel to high altitude regions on a yearly basis for military, recreational, and occupational purposes: AMS will be attenuated, and exercise performance and sleep will be significantly improved if individuals reside at moderate altitudes (i.e., 1800–2200 m) prior to ascending to high altitude.

## Conclusions

In conclusion, long-term moderate-altitude residence is associated with ventilatory and hematologic acclimatization that decreases the severity and prevalence of AMS in men following rapid ascent to 4300 m. These AMS results in combination with the previously reported improvements in physical performance indicate that residence at moderate altitude is very effective in sustaining health and performance upon rapid ascent to high altitude.

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## Author Disclosure Statement

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